

REASONS FOR BELIEVING THAT THE ONLY WAY IN NATURE¹ FOR YELLOW FEVER TO BE CONTRACTED BY MAN IS FROM THE MOSQUITO.

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This article is intended mainly for the busy medical man, who from want of time and lack of opportunity, has not kept up with the details of the remarkable revolution which has taken place during the last few years in our knowledge of the etiology and prevention of yellow fever.

Havana, the chief focus and home of yellow fever, was constantly afflicted by that disease, never a month without deaths from it, from 1762 to September, 1901, a period of about 140 years. Eight months subsequent to the beginning of the American anti-mosquito sanitary work, which was based entirely upon the mosquito idea of the propagation of that disease, yellow fever had disappeared altogether from Havana, and since, up to the present time—an interval of 14 months, embracing two autumns and a summer—not a single case of the disease has occurred in that city. The intervening summer was an unusually hot one, and the city contained an unusually large number (at least 40,000) recently arrived non-immunes—just the conditions, which under the former regime must inevitably have produced a severe epidemic of yellow fever.

Sanarelli's proposed solution of the yellow fever problem, of which we had such high hopes four or five years ago, has been proven untenable by numerous high authorities and skilled investigators. The United States Army Yellow Fever Commission, composed of Major Walter Reed and Drs. Carroll, Lazear and Agramonte, United States Army, which visited Havana first in the early summer of 1900 investigated its claims and found that:

"First—The bacillus icteroides, Sanarelli, stands in no causative relation to yellow fever, but when present should be considered as a secondary invader in this disease.

"Second—The mosquito serves as the intermediate host for the parasite of yellow fever."

This commission returned to the United States the same summer, two of its brave members having had yellow fever, from which one of

¹ Yellow fever can with great certainty be produced by inoculating non-immunes with blood taken from persons affected with that disease; but, for obvious reasons, this cannot be called a natural method.

them, Dr. Jesse W. Lazear, died, thereby adding one more noble name to the long roll of medical martyrs who have yielded up their lives trying to help their fellow-men.

The latest utterance I have read about the *B. icteroides*, that of Dr. Porthier, a member of the recent United States Public Health and Marine-Hospital Commission on the "Investigation of the Yellow Fever and Mosquitoes in Veracruz," is, in part, as follows:

"The *B. Sanarelli* was doomed. The work of Reed and Carroll as to the transmission of yellow fever by the *Stegomyia fasciata* has been entirely corroborated." (Jour. Am. Med. Asso., Nov. 8, 1902, p. 1207).

In 1881, Dr. Carlos J. Finlay, a scholarly scientist, a British subject, born in Cuba, and a resident of Havana, promulgated the theory (now an established fact), of the transmission of yellow fever by the mosquito, and singled out the guilty species, now called *Stegomyia fasciata*. For many years subsequently he conducted experiments and published numerous articles attempting to convince the medical profession of the correctness of his views. In one of his contributions, read at Buda-Pesth in 1894, he recommends the following measures against the propagation of yellow fever through mosquitoes, which from our present point of view we may call prophetic:

"First—To prevent those insects from stinging yellow fever patients.

"Second—To destroy as far as possible the mosquitoes which have been infected. * * *

"Third—Finally, to consider any place unsafe so long as the last mosquitoes which have stung yellow fever patients may be alive in it." * * *

The beginning of this philosophic work of Finlay antedated by two or three years any of the mosquito-malarial theories and demonstrations. It occurred about the same time (but altogether independently) as the discovery by Sir Patrick Manson of the transmission of the *filaria nocturna*—the worm which causes *elephantiasis arabum*—by mosquitoes.

The brilliant work of Ronald Ross—1895-1899—Grassi, Marchiafava, Celli, and others, especially that of the first-named scientist, establishing the cognate fact of the conveyance of malaria by the *Anopheles* mosquito had great influence in leading to the demonstration of the transmission of yellow fever by mosquitoes.

The clear-cut scientific observations and classical contributions of Surgeon H. R. Carter, United States Marine-Hospital Service, showing the interval (about two weeks) which occurs in houses between the first (infecting) case and the first group of cases secondarily infected; so interesting and impossible to explain by the fomites theory,

are now readily understood in the light of our present knowledge of the elaboration of the yellow fever poison in the body of the mosquito—that process requiring not less than 12 days.

The Army Medical Commission, presided over by Walter Reed, First Vice-President of this Association for the present year, whose recent untimely death—an incalculable loss to the medical profession and to humanity—we are now mourning, returned to Cuba in the autumn of 1900, and resumed their mosquito-yellow-fever investigations. The reasons given by Major Reed for taking up the mosquito problem were:

1. Finding that Sanarelli's bacillus had nothing to do with the causation of yellow fever.

2. The unsatisfactoriness of the proof of the propagation of the disease by fomites.

3. The perfect demonstration by Ronald Ross, and the Italian observers, that the *Anopheles* mosquito is the intermediate host and conveyer to man of the malaria parasite.

4. Carter's establishment, published in May, 1900, of the two to three weeks' interval between the first (infecting) case of yellow fever in a house or ship and the subsequent outbreak or group of cases.

This Commission's subsequent work continued during the remainder of the autumn, and following winter, 1900-01.

They produced 13 cases of yellow fever by having non-immunes stung by contaminated mosquitoes (*Stegomyia fasciata*). Three other cases were produced by direct inoculations of the blood of yellow fever patients.

These experiments were conducted in such a manner as to make it impossible for the patients to have contracted the disease in any other way. Each case was diagnosed positively as yellow fever by the official Yellow Fever Commission of Havana, composed of such eminent experts as Finlay, Gorgas, Guitéras and Albertini; whose function was to make diagnosis of all cases reported as suspicious of being yellow fever.

The famous paper read by Major Walter Reed before the Pan-American Medical Congress, Havana, February, 1901, describes their flawless procedures, which leave no possible room for doubt that yellow fever is contracted by man from the mosquito. Nevertheless, the medical profession of Havana remained unconvinced, and similar experiments, with similar results, were repeated during the succeeding year inside the city of Havana, at Las Animas Hospital, of which I was at the time the director. An "Inoculation Station" was established in said hospital, under the immediate charge of Dr. Juan Guitéras. Eight experimental cases, in all, were produced at Las

Animas. The diagnoses were verified by the Yellow Fever Commission of Havana. During their illness the patients were unrestrictedly visited by the leading physicians of Havana.

Thus it will be seen that 21 well-marked cases of yellow fever—Reed's 13, and Guitéras' 8—representing the different varieties and intensities of the disease, were unquestionably caused by the bite of contaminated mosquitoes, within the established incubation period (one to six days) with almost mathematical precision. Three of these mosquito-borne cases proved fatal, and the necropsy revealed the characteristic lesions of yellow fever. The demonstration of the fact that yellow fever is produced by the mosquito was then, for the first time, accepted as complete by the physicians of Havana.

It now remains to consider whether or not yellow fever is capable of being produced in nature in any other way. This question is so important, and doubt in regard to it so natural, that I shall give in detail two sets of experiments—one conducted for its elucidation at Quemados, by the United States Army Commission; the other, at Las Animas Hospital, by myself. In these two sets of experiments every possible effort was made to cause yellow fever by fomites, the result in each instance being a signal failure.

"There was erected at Camp Lazear (one mile from Quemados, and about seven miles from Havana), a small frame house with a cubic capacity of about 2800 feet, tightly ceiled and battened, provided with small windows, so as to prevent a thorough circulation of air through the house, and with wooden shutters to prevent the disinfecting qualities of sunlight. The windows were closed by permanent wire screens with a 5-millimetre mesh. The vestibule was protected by a solid door and a wire screen door, and the inner entrance by a second wire screen door. In this way the passage of mosquitoes into the room was effectively excluded. The average temperature was kept at 76.2° F. for a period of 63 days, and precaution was taken to maintain sufficient humidity of the atmosphere. On November 30th, three large boxes filled with sheets, pillow-slips, blankets and so on, contaminated by contact with cases of yellow fever and their discharges were received and placed in the room. Most of these articles had been taken from the beds of patients sick with yellow fever in Havana. Many of them had been purposely soiled with the excretions of patients. These soiled sheets, pillow cases and blankets were used in preparing the beds in which the members of the hospital corps slept. During 63 days this building, thus furnished, was occupied by seven non-immune persons. Three of them occupied the room each night for 20 days. Later, a fourth box of clothing and bedding was added, some of it purposely soiled with the bloody stools

of a fatal case of yellow fever. Two of them occupied beds from December 21st to January 10th, every night wearing the very garments worn by yellow fever patients throughout their entire attacks, making use exclusively of their much soiled pillow-slips, sheets and blankets. At the end of 21 nights they went into quarantine (as had the former three) and were released five days later. Two other non-immunes occupied the same beds for 20 days more. The attempt, therefore, which was made to infect this building and its seven non-immune occupants during a period of 63 days was an absolute failure; all seven were released from quarantine in excellent health."—From "Mosquitoes," by Howard.

Later on some of these same men were bitten by yellow fever mosquitoes, and promptly came down with yellow fever.

These fomites experiments have been pronounced inconclusive by many medical men upon the grounds, chiefly, that they were conducted during the winter season, and in the country, outside the city.

The following extract from my "Report of Experiments with Yellow Fever Fomites at Las Animas Hospital, Havana, Cuba, September-November 1901" read before the International Sanitary Congress, Havana, February 10, 1902, sets forth the principal details and results of the second set of experiments, in which the objections urged to the first set are removed.

"Two rooms were selected in buildings constructed of masonry, about 150 meters apart, both within the hospital enclosure. These rooms were thoroughly renovated, provided with doors and windows of wire gauze—mosquito proof—being further protected by vestibules of the same material. All the cracks and rough places in the walls, ceilings and floors were smoothly sealed; and an abundance of pyrethrum powder burned in the rooms, in order to preclude the possibility of the presence of any mosquitoes. One of these rooms was called the observation room, and the other, the experimental room.

The observation room was fitted out with furniture, utensils, bedding and clothing which had been thoroughly disinfected, so that there could be no suspicion of extraneous contamination.

In the experimental room were placed numerous bundles containing clothing, bed clothes and bedding which had recently been used in the sick rooms and on the persons of patients ill with yellow fever; much of it badly soiled with discharges and excreta of said patients. These articles had been used by Ventura Trillo Ramos and Juan Lago, at the private hospital, "La Benefica," Havana (usually an infected place) and by patients in the hospital at Columbia Barracks, Quemados, Cuba. All these cases had been diagnosed as yellow fever in their

respective hospitals, and confirmed as such by the yellow fever commission of Havana. The cases of Juan Lago and Vicente Real were fatal, the latter having presented during its course and at the autopsy unmistakable appearances of malignant yellow fever.

Eight men, newly arrived on the island, five Spanish, two Italian and one English, all healthy, by no possibility immune were procured from the immigration station, Tricornia, across the bay from Havana, as subjects for our experimentation.

Two of these men were placed in the observation room on September 27, and confined there for more than a week. At the end of that period they were transferred to the experimental room, where they were kept for seven days. They were then released and given light work in the hospital grounds. When they were removed from the observation room, two others of the subjects were placed therein for seven days—afterwards taking their turn in the experimental room for the same length of time. In this way, all eight of the men, after rigid physical examination, went through the observation and experimental rooms, two by two, emerging therefrom in good health, and remaining so until all possibility of having contracted yellow fever had passed away.

While in the experimental room the subjects used, upon their persons for sleeping, the night shirts, pajamas, bedding, bed clothes, etc., above described, soiled with fecal dejections, black vomit and blood. From time to time other packages, containing similarly soiled fomites, were introduced and the subjects required to frequently shake them within the room. While in the observation room, the men were not allowed to leave it, except for necessary exercise, and then under guard. While in the experimental room, they were not allowed outside under any condition. Their food was carried to them, and there were guards over them night and day.

A careful clinical record was kept of each man during the 14 days he was kept in the observation and experimental room. The temperature, pulse, respiration, appetite, etc., of all eight continued practically normal throughout.

At the beginning of these proceedings, written invitations were sent to the physicians of Havana, requesting them to visit Las Animas at their pleasure, to observe the progress of the experiments.

I beg leave to call especial attention to the following facts in connection with these experiments, viz.:

1. They were conducted in the city of Havana itself, within whose beautiful limits, until recently, Cuba's yellow sorrow had run riot continuously for 139 years.

2. They were conducted in buildings, similar in construction and material (*mamposteria*) to those occupied by people of the poorer classes of the city—damp, poorly lighted, badly ventilated, floors on the level of the ground.

3. They were conducted at the season of the year when, in this latitude, the dreaded scourge is at its worst and does its most deadly work." Said period comprising the latter part of September, the whole of October, and the first part of November—the height of the yellow fever season at Havana.

Military Governor Wood, with his characteristically clear perception, appreciated, from its very beginning, the promise and importance of the mosquito-yellow fever work in Havana. He generously provided the funds for the experiments and for the large expenditures, sometimes \$35,000 a month, subsequently and consequently required by Major Gorgas, the chief sanitary officer, for the successful conduct of the anti-mosquito crusade. Major Reed, in the paper referred to above, expresses sincere thanks to "Major General Leonard Wood, U. S. V., without whose approval and assistance, these observations could not have been carried out."

For 140 years prior to the late Spanish-American war, Havana had never been free from yellow fever; the annual number of deaths from that disease having averaged from 500 to 1000, some years as many as 1600—largely among the Spanish soldiers, great numbers of whom were imported every year, up to 1898. During the first two years of American occupation the sanitary authorities devoted themselves energetically to putting the city in good hygienic condition, and especially to measures then considered most effective against yellow fever; such as the destruction and disinfection of fomites and localities supposedly infected by that disease. The result was a rapid decrease of all infectious diseases, except yellow fever, and an enormous diminution of the general mortality rate. Smallpox, which had been a terrible scourge under the Spanish administration, disappeared entirely in July, 1900, and has not returned since. Nevertheless, the amount of yellow fever in the city did not diminish along with other fevers, showing that ordinary sanitary measures had no effect upon it. There was more yellow fever in Havana during December, 1899, than in any December for several previous years. In 1900, there was a sharp epidemic, and in December of that year, there were 20 deaths from yellow fever in the city. In January, 1901, there occurred 24 cases in Havana. In February, 1901, Major Gorgas, having fully accepted the demonstration of the propagation of yellow fever by mosquitoes, turned all the energies of himself and his department to,

First—The protection of yellow fever patients from mosquitoes.

Second—The prevention of the infection of mosquitoes by yellow fever patients.

Third—The destruction, by fumigation, etc., of all possibly infected mosquitoes. And

Fourth—The abolition of all water barrels, pools and other breeding places of mosquitoes in Havana.

Practically no attention was paid to fomites, of which at the time there must have been a great abundance in the city. No attempt was made to get rid of fleas and bed-bugs, by which Havana is, at all times, infested. The result of this concentration upon the mosquito, and neglect of every other supposed cause of yellow fever, was a rapid subsidence of that disease until within less than eight months, the last case had occurred in the city, after which yellow fever disappeared entirely. Not a case of it has occurred in Havana since September 27, 1901; although during the summer and autumn just ended patients sick with yellow fever, contracted in Mexico and Central America, were frequently carried through the heart of the city from the ships by which they had been imported, to the yellow fever hospital. During their transportation from ship to shore, and along the streets, they were kept carefully covered with mosquito netting, and upon arriving at the hospital, were placed in wards made mosquito-proof by wire-gauze screens. In the same wards were treated, at the same time, non-immune patients, sick with other diseases, and they were attended by non-immune nurses. That yellow fever is contracted solely from the mosquito is now so firmly and universally believed in Havana, that no one has the slightest fear of patients affected with that disease, provided the said patients be protected from mosquitoes and the mosquitoes from them.

It is contended by the opponents of the mosquito doctrine that the disappearance of yellow fever from Havana may not have been due to Major Gorgas' active anti-mosquito measures; because yellow fever had frequently disappeared, for considerable periods, from Santiago and other Cuban cities. But the conditions were quite different in Havana and the smaller cities. In the latter, the number of non-immunes was always very small, and the epidemic of yellow fever in one of these soon ceased, on account of the consumption of susceptible material; whereas, in Havana, the commercial, military, and yellow fever center of the island, the number of non-immunes was always large, thousands of immigrants coming into it every year, constituting an uninterrupted and inexhaustible stream of fresh material for keeping up yellow fever in an epidemic form.

All of the many able, cultivated, trained American medical officers—among them such men as General Wood, Surgeon-General O'Reilly, Major Kean, Major Gorgas, Surgeon Carter, Surgeon Glennan, Captain Stark, and others, who were in Havana, and who had personal knowledge of the mosquito-yellow fever experiments and demonstrations made there, were, without exception, completely convinced that *yellow fever is transmitted to man exclusively by the mosquito*. This is exceedingly strong evidence, to my mind, of the correctness of the proposition stated in the title of this paper. Had our distinguished colleagues, who do not agree with us, been on the ground as we were; and seen with their own eyes, as we saw, the exactness and completeness of the proofs, I believe they would have been convinced, as we were.

The idea, held by some able and prominent medical men, that yellow fever may be transmitted by bed-bugs, fleas and other suctorial insects, is, in the light of our present knowledge of insects and disease, highly improbable. Bed-bugs and fleas are found all over the world, in all climates, and at all seasons of the year; whereas, yellow fever is restricted to certain tropical and sub-tropical regions, and prevails only in the summer and autumn.

Another highly significant fact, in this connection, is that while yellow fever was melting away like ice under a summer sun before Major Gorgas' anti-mosquito operations, the city of Havana was infested with bed-bugs, fleas, etc., galore; no attention being paid to them by the sanitary department, and that the same prevalence of these blood-suckers has continued throughout the subsequent 14 months, during which the city has remained free from yellow fever.

Although the germ of yellow fever has not been found (no more has that of smallpox) yet, the scientific and circumstantial evidence is practically positive that it is an animal parasite, whose cycle requires a certain length of time, and is very similar to that of the malarial parasite. We know that the yellow fever germ goes from man to the *Stegomyia* mosquito and from the *Stegomyia* back to man. No instance has ever been advanced in which there seemed to me even a possibility that yellow fever had been transmitted by bed-bugs, fleas or flies. Certain it is that no such case has occurred in Havana during the past 14 months, in which yellow fever has been absent from that city, although, as shown above, unequalled opportunities for such an occurrence have there been constantly in existence.

Carter, in a very able contribution (Yellow Fever Institute Bulletin, No. 11) sums up as follows:

"For the belief that yellow fever is conveyed in nature *only* by a host, and doubtless a mosquito host, we have,

"First—The analogy of other diseases conveyed by insect hosts.

"Second—That all facts observed about the propagation of yellow fever agree with the necessary deductions of this theory.

"Third—No other theory explains all the facts observed of its propagation."

The fact that so many, perhaps all, of the peculiarities and problems of yellow fever, impossible to understand formerly, are explainable and capable of solution by what we know of mosquitoes and their relation to disease, is highly interesting and important. A few of these are:

Its singularly restricted area; its dislike for altitude, upper stories, plateaus, mountains, etc.; its partiality for the sea coast and low-lying districts; its incommunicability from man to man; the meaning of "place infection"; the interval, two to three weeks, between first (infecting) case and subsequent group of cases (Carter); its frequent appearance at sea several weeks after vessels had left port; its arrest by frost and cold weather; its survival through winters; its absence from Asia and India, etc.

Of the problems elucidated by the discovery of the mosquito origin of yellow fever, I cite that of the knottiest of them all, *the second outbreak on board the U. S. S. Plymouth, in 1879* (utterly inexplicable to me under the fomites, or any other theory). The *Plymouth* sailed from New England early in October, 1878; arrived at St. Thomas, W. I. (a yellow fever stronghold), October 21st, where she went alongside the wharf and coaled ship, remaining until October 25th. The officers and stewards were allowed to go on shore during this time. On the 25th, she went to Frederickstadt, Santa Cruz. November 4th, while at Frederickstadt, a case of yellow fever appeared on board. Between the 4th and 7th, seven cases occurred on board. On the 7th, the *Plymouth* started north, after which no fresh cases occurred in the ship. December 1st, she reached Portsmouth, New Hampshire, where the weather is usually cold at that season of the year. From Portsmouth she went to the nearby city of Boston, where she was emptied of her crew and stores, opened up and frozen out during January and a part of February, 1879. The vessel had been several times fumigated with burning sulphur. February 12th, 1879, she was recommissioned, and, on March 15th, started back to the West Indies. March 19th, "the damp berth-deck became very warm; a tropical condition prevailed." March 21st, immediately after reaching the tropics, and before she had touched at any port, yellow fever broke out among her crew.

The solution afforded by the mosquito doctrine is simple and satisfactory. The *Plymouth* left the West Indies November 7, with several fresh yellow fever cases, and, doubtless, with numerous contaminated mosquitoes on board. So soon as she entered winter weather, about December 1st, the infected mosquitoes went into hibernation and remained torpid until they re-entered the tropics, when some of them became active and stung certain of the men, thereby giving two of them yellow fever.

That mosquitoes hibernate is a well-known fact. Theobald, in his standard monograph, states that mosquitoes hibernate in the extreme cold of the arctic regions; that the gravid females seek shelter as soon as the weather becomes cold, lie dormant all winter, and deposit their eggs in early spring. Howard, the highest American authority upon the subject, says in his capital work, "Mosquitoes," page 6: "Mosquitoes hibernate in the adult condition." In conversation with this distinguished entomologist in Washington the other day (November 22, 1902) Howard used these words, which I took down verbatim: "The *Stegomyia* hibernates in the adult stage. I have a strong suspicion that it hibernates in the egg stage also."

Too much admiration cannot be accorded to Major Gorgas for the superb manner in which he accomplished the deliverance of Havana from yellow fever. In planning and conducting this creative work, without any precedent to guide him, he showed not only consummate administrative and executive ability and foresight, but, also, genius of a high order. After it was finished, it was impossible for us to look back upon it and point out any particular in which the work could have been improved.

At the recent meeting of the Conference of State and Provincial Boards of Health of North America, at New Haven, Conn., it was resolved concerning Major Gorgas' sanitary redemption of Havana, that, "we regard (it) as one of the most brilliant achievements of the application of sanitary science to public health work ever accomplished."